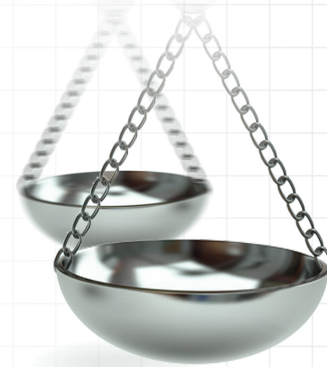




Cost minimization analysis of catheter ablation for paroxysmal atrial fibrillation by catheter technology

Jose Osorio¹, Ryan J Imhoff^{*,2}, Peter J Mallow^{2,3}, Tina D Hunter², Laura Goldstein⁴, Anil Rajendra¹ & Gustavo Morales¹

¹Cardiac Electrophysiology, Grandview Medical Center, Birmingham, AL, USA

²Real World Evidence, CTI Clinical Trial & Consulting Services, Covington, KY, USA

³Department of Health Services Administration, Xavier University, Cincinnati, OH, USA

⁴Health Economics & Market Access, Biosense Webster, Inc. Irvine, CA, USA

*Author for correspondence: Tel.: +1 513 598 9290; Fax: +1 513 598 3426; rimhoff@ctifacts.com

Aim: Compare the 1-year costs of three catheter ablation technologies for the treatment of paroxysmal atrial fibrillation (PAF). **Materials & methods:** A decision tree model was developed to estimate 1-year hospital costs associated with an index and potential repeat PAF ablation procedure using the Thermocool® Smarttouch® Catheter (ST), Thermocool SF Catheter (SF) or Arctic Front Advance Cryoballoon (CB). Model parameters were estimated using the results of two recently published studies. **Results:** The ST resulted in average per-patient savings for combined inpatient and outpatient populations of US\$1488 and US\$4494 compared with SF and CB, respectively. These cost savings were greater in the inpatient setting. **Conclusion:** The 1-year expected hospital visit costs for PAF ablation were lower with ST than with SF or CB.

First draft submitted: 15 October 2018; Accepted for publication: 4 December 2018; Published online: 10 January 2019

Keywords: atrial fibrillation • decision tree simulation model • radiofrequency ablation

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the USA, affecting between 2.7 and 6.1 million people [1], with these numbers expected to double over the next 25 years [1]. AF presents a significant burden to the United States (US) healthcare system, with more than 750,000 AF-related hospitalizations each year [2]. The high prevalence and hospitalization rates result in considerable economic burden, costing an estimated US\$6 billion each year in the US [3]. This equates to an incremental cost per patient of US\$8705 annually compared with similar patients without AF [3].

Current consensus treatment guidelines recommend the use of catheter ablation in AF patients that are refractory to or cannot tolerate medical therapy, with several systematic reviews supporting the safety and efficacy [1,4–8]. Catheters with two distinct energy sources – radiofrequency (RF) and cryoablation – are approved for percutaneous AF ablation in the USA. While the acute procedural success rate for ablation is very high, AF recurrence rates of 20–40% have been reported [5,9,10]. The lowest rates have been observed with contact force (CF) sensing RF and second-generation cryoablation technologies, with similar rates seen in these two technologies [10]. A number of AF recurrences eventually require reablation, which is most commonly due to pulmonary vein reconnection [1].

In 2014, the Thermocool® Smarttouch® Catheter (Biosense Webster, Inc., CA, USA; ST) was approved by the US Food and Drug Administration (FDA) for the treatment of paroxysmal atrial fibrillation (PAF). The ST is an RF ablation catheter that employs CF sensing technology to provide valuable feedback on force, energy level and ablation time. Use of the ST catheter can lead to high freedom from recurrence at 1-year postprocedure, and the rate of success has been shown to increase with the percentage of time that an operator stays within their targeted stability range [11].

A limited number of real-world studies compare the effectiveness of the ST catheter with prior RF catheters or cryoablation catheters in the US. However, an analysis by a single high-volume site showed that ST significantly reduced the rate of repeat ablation procedures during 1 year after index AF ablation compared with both prior RF and second-generation cryoablation technologies [15].

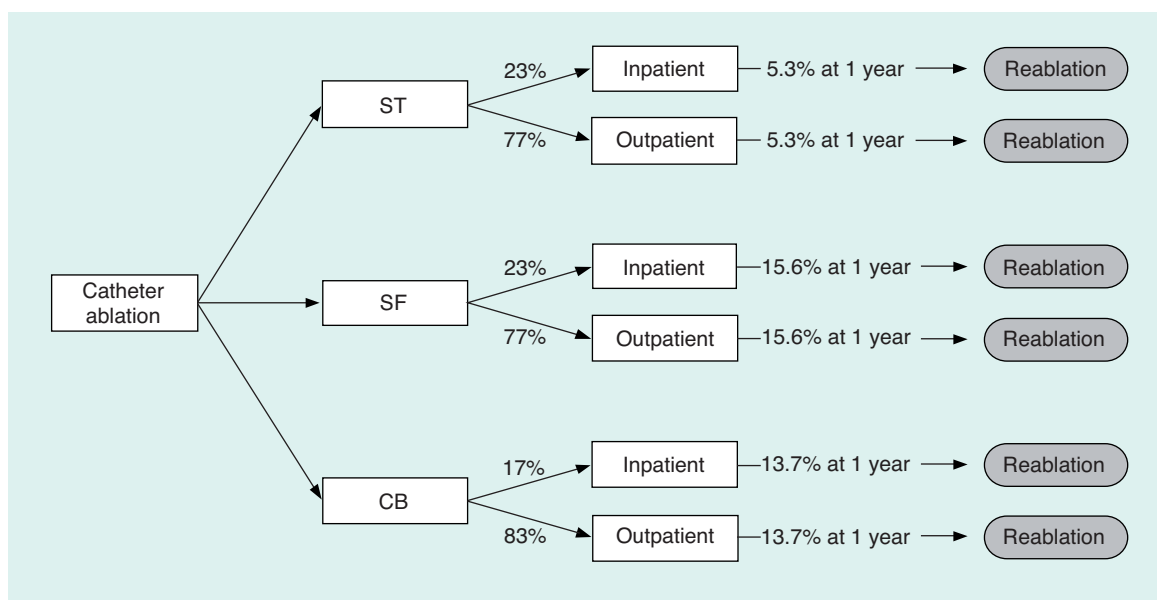


Figure 1. Model scaffold. The above illustration represents Model 1, which includes both inpatient and outpatient procedures. For Models 2 and 3, the outpatient/inpatient nodes were removed. CB: Arctic Front Advance Cryoballoon; SF: Thermocool SF Catheter; ST: Thermocool Smarttouch Catheter.

Given the economic burden of AF, it is important to understand which of the current treatment technologies results in the lowest overall ablation costs. A 2016 study by Hunter *et al.* showed that non-CF RF ablations had lower procedure visit costs than cryoablations; [13] however, the study did not factor in downstream costs of each technology into the analysis via consideration of differences in repeat procedure rates.

The objective of this study was to evaluate the costs of two generations of RF ablation catheters, the ST catheter and the Thermocool SF Catheter (Biosense Webster, Inc.; SF), along with the second generation cryoballoon catheter, the Arctic Front Advance Cardiac Cryoablation Catheter (Medtronic PLC, Dublin, Republic of Ireland; CB). This study estimates the cost minimizing strategy for AF ablation from the hospital perspective by comparing ST versus SF and ST versus CB across inpatient and outpatient procedure settings.

Materials & methods

A cost-minimization analysis was performed to estimate the expected 1-year costs of treating PAF with catheter ablation. The ST treatment arm was compared separately with the SF and CB arms. This type of analysis was chosen because the acute procedural success and adverse event rates at the ablation procedure were similar across the three catheter technologies [15]. A decision tree simulation model was developed to estimate the expected costs for each of the technologies. This method was chosen due to the short-time horizon, population-level analysis and straightforward nature of the outcomes [14].

Model structure

Three models were developed to assess alternative scenarios. The base case model included a mix of inpatient and outpatient procedures reflective of a typical hospital practice (Model 1), while the inpatient (Model 2) and outpatient (Model 3) procedures were also modeled separately to better assess the differences in these care settings. For the initial procedure, patients were ablated with ST, SF or CB. The use of multiple technologies during a procedure was not considered. A visual representation of the decision tree model is shown in Figure 1. The outcomes of interest were the cost of the initial catheter ablation visit and the cost of repeat ablation during 1-year postablation. Acute procedure-related serious complications were infrequent and occurred at similar rates between the three cohorts (SF: 2/32 [6%]; ST: 9/232 [4%]; CB: 1/59 [2%]; $p = 0.5311$) [13,15].

All modeling was performed using TreeAge Pro 2017 (TreeAge Software, Inc., MA, USA) and validated using Microsoft Excel 2016 (Microsoft, Inc., WA, USA).

Table 1. Parameter values.

Model parameter	Model inputs			
	Default	SE	Low [†]	High [†]
ST				
Inpatient price premium (US\$)	705	–	–	–
Outpatient price premium (US\$)	853	–	–	–
Inpatient procedure cost (US\$)	24,665	608	23,450	25,881
Outpatient procedure cost (US\$)	22,773	198	22,378	23,168
Reablation rate (%)	5.3	1.6	3.7	6.9
Proportion of inpatient procedures (%)	23.2	–	20.9	25.6
SF				
Inpatient procedure cost (US\$)	23,960	608	22,745	25,176
Outpatient procedure cost (US\$)	21,920	198	21,525	22,315
Reablation rate (%)	15.6	6.4	9.2	22.0
Proportion of inpatient procedures (%)	23.2	–	20.9	25.6
CB				
Inpatient procedure cost (US\$)	30,858	663	29,532	32,184
Outpatient procedure cost (US\$)	24,791	254	24,284	25,298
Reablation rate (%)	13.7	4.5	9.2	18.2
Proportion of inpatient procedures (%)	17.3	–	15.6	19.1

All cost values are reported in 2017 USD.
[†]For cost parameters, the low/high values were calculated as ± 2 SE, respectively. For clinical parameters, the low/high values were calculated as ± 1 SE, respectively.
 CB: Arctic Front Advance Cryoballoon; SE: Standard error; SF: Thermocool SF Catheter; ST: Thermocool Smarttouch Catheter.

Clinical parameters

Repeat ablation rates during the first year after the initial catheter ablation were populated with estimates from a nonrandomized, retrospective single site study previously presented at the European Heart Rhythm Association Congress in 2017 [15]. The study evaluated 383 ablations (277 ST, 43 SF and 63 CB) performed between July 2013 and June 2016 at a single electrophysiology practice. The study's Kaplan–Meier estimates of repeat ablation rates at 1 year are shown in Table 1. Patient characteristics for this population are provided in a Supplementary Table.

A simplifying and economically conservative assumption was made that all repeat ablation would be performed using an SF catheter, and thus follow-up visit costs were standardized regardless of the initial ablation technology used. In addition, the setting of the initial ablation was assumed to have no effect on a patient's need for a repeat procedure; thus, reablation rates for a given catheter were assumed to be the same after inpatient and outpatient procedures.

Costs

Cost estimates were obtained from a published retrospective analysis of adult patients with AF [13]. The study evaluated 2537 ablations performed during 2013 and 2014 at hospitals submitting data to the Premier Perspective Hospital Database. To estimate the visit cost for procedures using ST, which had not been adopted in the USA as of the time of that study, the expected price premium for an ST catheter versus an SF catheter was provided by Biosense Webster, Inc. The cost estimates used for the models are listed in Table 1. All cost data were adjusted to 2017 dollars based on the Consumer Price Index – Medical Care, published by the US Bureau of Labor Statistics [16].

Sensitivity analysis

One-way sensitivity analysis

A one-way deterministic sensitivity analysis was conducted by varying each model parameter individually and observing the effect on the results in order to assess the impact of the individual model parameters and the robustness of the findings. Reablation rates were varied by ± 1 standard error (SE), procedure costs were varied by ± 2 SE, and the ratios of inpatient to outpatient procedures were varied by $\pm 10\%$. The SE for each variable is shown in Table 1. For the reablation rates, the SE reported is the SE of the Kaplan–Meier product limit estimate. For cost variables, SEs of the population estimates were calculated from the reported standard deviations and sample sizes. The one-way sensitivity analyses (SA) were conducted separately for each of the three models.

Probabilistic sensitivity analysis

Monte Carlo probabilistic SA were performed for three models to further evaluate the robustness of the results. Both first-order and second-order uncertainty were tested by running a simulation of 5000 trials, each of which consisted of 50,000 hypothetical patients. This sensitivity analysis was used to estimate the proportion of simulated trials for which ST had lower costs than SF, and for which ST had lower costs than CB.

Cost values were sampled from the distribution of the mean cost, as defined by the means and SEs of the visit costs. The mean cost was assumed to be normally distributed based on the central limit theorem. For reablation rates, a triangular distribution was assumed. The distribution was estimated using the proportion reported by Osorio *et al.* as the most likely value and ± 1 SE as the minimum and maximum values [15].

Results**ST versus SF**

The full cohort of PAF patients having a catheter ablation using either ST or SF (Model 1) have expected 1-year ablation visit costs (index ablation plus repeat ablation) of US\$24,400 and US\$25,888, respectively (Figure 2). Consequently, the expected cost savings is US\$1488 per patient treated with ST versus SF in 1 year after the index ablation procedure.

Patients who receive a catheter ablation in the inpatient setting (Model 2) have expected costs of US\$25,935 and US\$27,698 with ST and SF, respectively. Consequently, the expected 1-year cost savings with ST is US\$1763.

Similarly, patients receiving an ablation in an outpatient setting (Model 3) have expected 1-year ablation costs of US\$23,935 and US\$25,340 with ST and SF, respectively, resulting in an expected savings of US\$1405 per patient in the ST cohort.

ST versus CB

Patients undergoing a PAF catheter ablation in any setting (Model 1) with ST or CB catheters have expected average ablation visit costs (index ablation plus repeat ablation) of US\$24,400 and US\$28,894, respectively. Consequently, the expected 1-year cost savings are US\$4494 per patient treated with ST versus CB.

Patients receiving a catheter ablation in the inpatient setting (Model 2) have expected 1-year costs of US\$25,935 and US\$34,141 for ST and CB, respectively, leading to an expected cost savings of US\$8206 per patient treated with ST.

Patients ablated in an outpatient setting (Model 3) have expected 1-year ablation visit costs of US\$23,935 and US\$27,794 for ST and CB, respectively, with an expected savings of US\$3859 per patient treated with ST.

Sensitivity analysis*One-way sensitivity analysis*

The one-way SA conducted for the three models found that ST is cost saving compared with SF and CB at all tested parameter values. When comparing ST with SF and CB, respectively, the models were found to be most sensitive to SF reablation rates and CB reablation rates, with the exception of the inpatient only model (Model 2) comparing ST with CB, in which case the model was most sensitive to CB procedure cost. Tornado diagrams for each model showing the effects of changing each parameter value can be seen in Figure 3.

Probabilistic Sensitivity Analysis

In the probabilistic sensitivity analysis that evaluated ST versus SF, cost savings were observed in 100% of the iterations for each of the three models. Similarly, ST minimized costs 100% of the time in the inpatient model for ST versus CB. In the combined setting and outpatient models, ST minimized 1-year costs compared with CB 99.8% and 99.6% of the time, indicating that the model results were robust to expected variations in parameter values.

Discussion

With any new technology, it is important to evaluate the clinical effectiveness and impact on healthcare costs. The goal of this study was to evaluate the cost impact of an innovation in RF ablation technology for the treatment of PAF. The ST catheter has been shown to have significantly lower reablation rates than both SF and CB catheters when treating patients with PAF [15]. This study sought to explore how the differences in reablation rates contributed

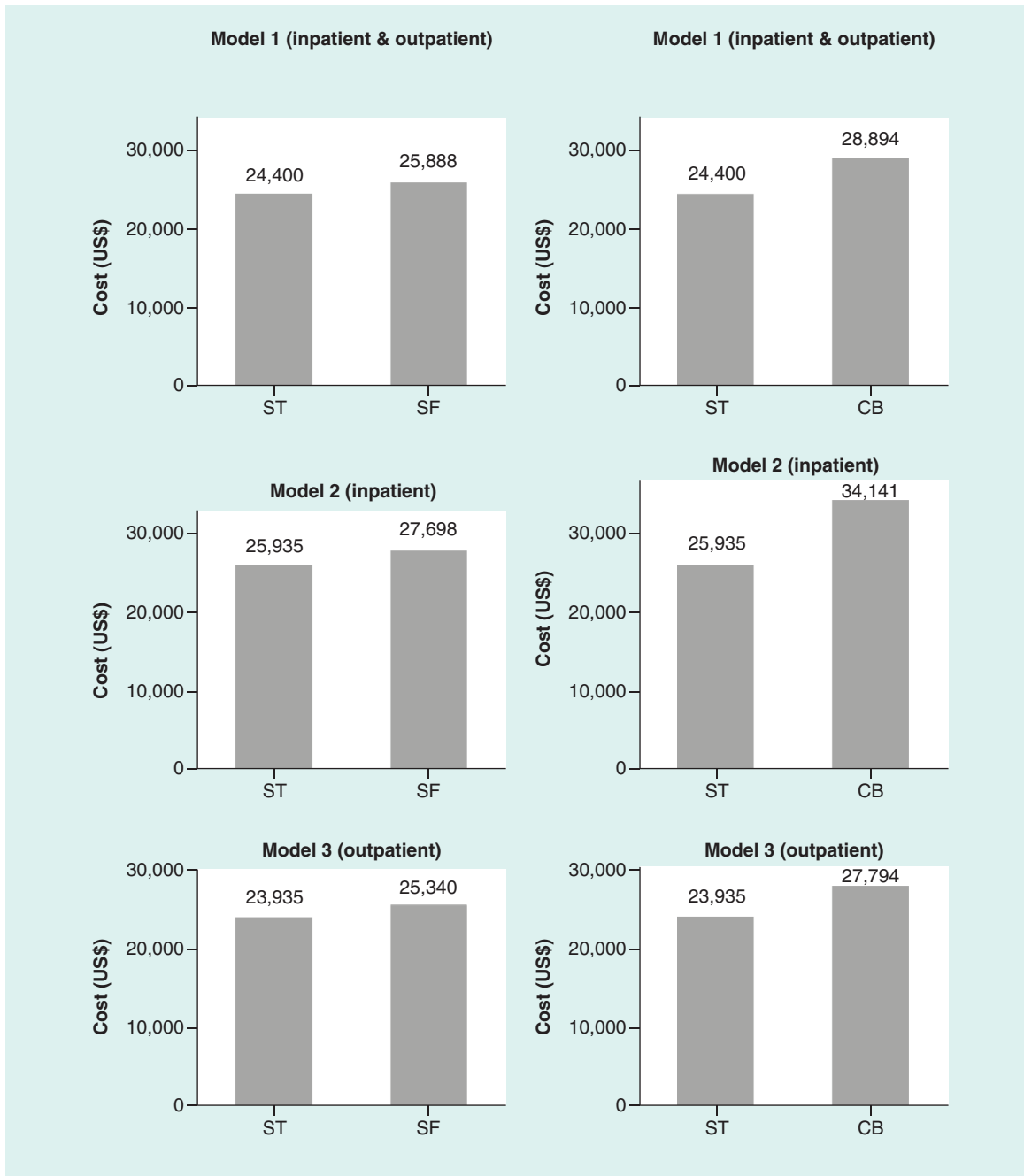


Figure 2. Base case cost minimization results. All cost values are reported in 2017 USD.
CB: Arctic Front Advance Cryoballoon; SF: Thermocool SF Catheter; ST: Thermocool Smarttouch Catheter.

to economic value by comparing the 1-year costs of PAF ablation with the ST catheter to both SF and CB catheters from the hospital perspective.

The results of this study found ST to be the cost minimizing strategy in all three models. The base case model, incorporating both inpatient and outpatient procedures, resulted in 1-year cost estimates of US\$24,400, US\$25,888 and US\$28,894 for ST, SF and CB, respectively. Cost savings with ST were greatest in the inpatient setting, particularly when compared with CB, where cost savings for inpatient procedures were more than double those for outpatient procedures. The ST versus CB cost savings were driven by the lower index procedure costs with ST combined with significantly lower repeat procedure rates within 1 year. Moreover, despite the slightly higher

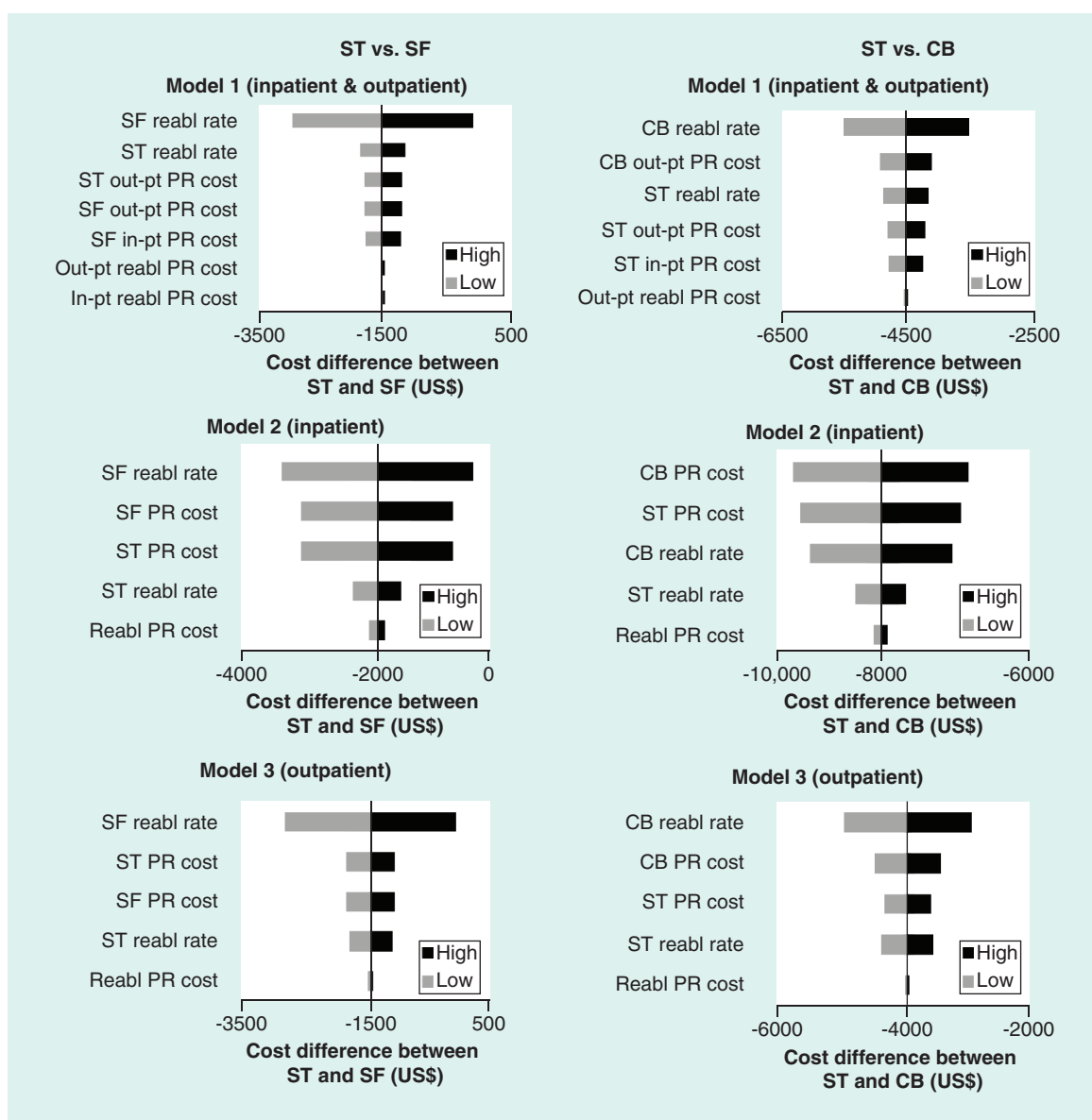


Figure 3. One-way sensitivity analysis tornado diagrams.

CB: Arctic Front Advance Cryoballoon; SF: Thermocool SF Catheter; ST: Thermocool Smarttouch Catheter.

index procedure cost of ST compared with SF, 1-year cost savings were realized due to substantially lower repeat ablation rates. Extrapolating the results of this study, in a center that performs 100 ablations per year, this amounts to US\$148,800 and US\$449,400 in annual cost savings by using ST instead of SF and CB, respectively.

The ST is a relatively new technology, receiving US FDA approval in 2014, so the real-world clinical and economic outcomes have not been studied extensively. The study by Osorio *et al.* found that in a real world population at a single high-volume site using a standardized workflow, ablations performed with a ST catheter led to significantly fewer reablations in the first 12 months than procedures performed with SF or CB catheters, with no significant difference between SF and CB [15]. In comparison, the FIRE AND ICE trial found no difference in 12-month efficacy between RF and CB ablation procedures [17]. The ST catheters comprised only a quarter of the RF cohort in this trial, and it was not powered to distinguish between the older and newer technologies.

One small single site study published in 2013 reported hospital costs of US\$7482 higher, on average, for cryoablation procedures than RF ablation procedures [18]. The larger 2016 database study by Hunter *et al.*, which was utilized in this study, found adjusted visit costs of US\$6942 and US\$2889 higher for cryoablation than RF

ablation in the inpatient and outpatient settings [13]. Furthermore, a 2013 conference abstract describing a cost-consequence analysis comparing ST with non-CF RF catheters, based on clinical data from an Italian hospital, found that ST was a cost-saving technology [19], consistent with the findings of this study. To the authors' knowledge, this is the first cost analysis comparing ST with both SF and CB technologies.

Limitations

The clinical data used in this study are based on analysis of the results of a non-randomized single site experience. These data were used because published data from a multicenter or randomized study was not available. Moreover, this study was designed from the perspective of a US hospital. Consequently, the findings of this study may not be generalizable outside of these settings.

This model does not take into consideration the possibility for multiple repeat ablations in 1 year or use of multiple technologies during the initial procedure. However, multiple repeat ablations within a single year are rare in PAF and did not occur in the study population that was utilized for repeat ablation rates. In addition, the model assumed that repeat ablation rates were the same for both inpatient and outpatient procedures and that all patients were reablated using SF catheters.

Conclusion

In a high-volume US site, the use of the ST catheter for ablation of PAF resulted in a substantial reduction in 1-year expected hospital visit costs for index and repeat ablations compared with SF or CB, driven by lower 1-year reablation rates.

Summary points

- This study estimated the lowest cost catheter ablation technology for paroxysmal atrial fibrillation by comparing index ablation and 1-year reablation costs for the Thermocool Smarttouch (ST) Catheter versus the Thermocool SF (SF) and Arctic Front Advance (CB) Catheters.
- A deterministic decision tree simulation model was developed from the hospital perspective. Costs assessed for all three cohorts included the initial catheter ablation visit and the first reablation visit for any patient requiring reablation within 1 year.
- Three models were developed to estimate costs across inpatient and outpatient settings (Model 1) as well as within inpatients only (Model 2) and outpatients only (Model 3).
- The 1-year reablation rates were populated with real world data estimates based on 383 ablations (277 ST, 43 SF and 63 CB) performed between July 2013 and June 2016 at a single high-volume electrophysiology practice.
- The average costs of catheter ablation visits using SF or CB were populated from a 2017 study by Hunter *et al.* that utilized the Premier Hospital database, evaluating 2537 ablations performed during 2013 and 2014 at hospitals using both technologies.
- One-way and probabilistic sensitivity analyses were performed to test the robustness of the cost minimization results.
- The ST led to cost savings of US\$1488, US\$1763 and US\$1405 per patient treated versus SF in combined the inpatient and outpatient settings (Model 1), for inpatients only (Model 2) and for outpatients only (Model 3), respectively.
- When compared with CB, ST led to cost savings of US\$4494, US\$8206 and US\$3859 per patient treated in the combined inpatient and outpatient settings (Model 1), inpatient setting only (Model 2), and outpatient setting only (Model 3), respectively.
- Sensitivity analysis showed that the models were generally most sensitive to reablation rates within the SF and CB cohorts and found the results robust to changes in parameter values.
- These results suggest that the use of the ST catheter for ablation of paroxysmal atrial fibrillation could result in a substantial reduction in expected 1-year hospital costs for index and repeat ablations compared with SF or CB.

Author contributions

All authors contributed to revising the manuscript have approved the final version of the manuscript and are accountable for all aspects of the work. RJ Imhoff and PJ Mallow drafted the manuscript; RJ Imhoff and PJ Mallow with TD Hunter were responsible for design, analysis and interpretation of the economic model. J Osorio, L Goldstein, A Rajendra and G Morales contributed to the concept of the economic model and collection of the clinical data used in the model.

Financial & competing interests disclosure

This study was funded by Biosense Webster, Inc. J Osorio is a consultant to Biosense Webster, Inc. and Boston Scientific Corp. G Morales is a consultant to Biosense Webster, Inc. RJ Imhoff and TD Hunter are employees of, and PJ Mallow is a consultant to, CTI Clinical Trial and Consulting Services, which is a consultant to Biosense Webster, Inc. L Goldstein is an employee of Biosense Webster, Inc. A Rajendra has no disclosures. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Open access

This work is licensed under the Attribution-NonCommercial-NoDerivatives 4.0 Unported License. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>

References

Papers of special note have been highlighted as: • of interest

1. January CT, Wann LS, Alpert JS *et al.* 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J. Am. Coll. Cardiol.* 64(21), e1–e76 (2014).
2. Agency for Healthcare Research and Quality. Weighted national estimates. HCUP National Inpatient Sample [online]. <http://hcupnet.ahrq.gov/HCUPnet.jsp>
3. Kim MH, Johnston SS, Chu BC, Dalal MR, Schulman KL. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. *Circ. Cardiovasc. Qual. Outcomes* 4(3), 313–320 (2011).
4. Bonanno C, Paccanaro M, La Vecchia L, Ometto R, Fontanelli A. Efficacy and safety of catheter ablation versus antiarrhythmic drugs for atrial fibrillation: a meta-analysis of randomized trials. *J. Cardiovasc. Med.* 11(6), 408–418 (2010).
5. Calkins H, Reynolds MR, Spector P *et al.* Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. *Circ. Arrhythm. Electrophysiol.* 2(4), 349–361 (2009).
6. Nair GM, Nery PB, Diwakaramenon S, Healey JS, Connolly SJ, Morillo CA. A systematic review of randomized trials comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation. *J. Cardiovasc. Electrophysiol.* 20(2), 138–144 (2009).
7. Parkash R, Tang AS, Sapp JL, Wells G. Approach to the catheter ablation technique of paroxysmal and persistent atrial fibrillation: a meta-analysis of the randomized controlled trials. *J. Cardiovasc. Electrophysiol.* 22(7), 729–738 (2011).
8. Piccini JP, Lopes RD, Kong MH, Hasselblad V, Jackson K, Al-Khatib SM. Pulmonary vein isolation for the maintenance of sinus rhythm in patients with atrial fibrillation: a meta-analysis of randomized, controlled trials. *Circ. Arrhythm. Electrophysiol.* 2(6), 626–633 (2009).
9. Calkins H, Hindricks G, Cappato R *et al.* 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm* 14(10), e275–e444 (2017).
10. Jiang J, Li J, Zhong G, Jiang J. Efficacy and safety of the second-generation cryoballoons versus radiofrequency ablation for the treatment of paroxysmal atrial fibrillation: a systematic review and meta-analysis. *J. Intervent. Cardiac Electrophysiol.* 48(1), 69–79 (2017).
11. Natale A, Reddy VY, Monir G *et al.* Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. *J. Am. Coll. Cardiol.* 64(7), 647–656 (2014).
12. Osorio J, Hunter TD, Buben RS, Rajendra A, Arciniegas J, Morales G. Efficiency and effectiveness gains in paroxysmal atrial fibrillation ablation using a standardized workflow to optimize contact force technologies. *J. Atr. Fibrillation* (Under Review).
13. Hunter TD, Palli SR, Rizzo JA. Cost comparison of radiofrequency catheter ablation versus cryoablation for atrial fibrillation in hospitals using both technologies. *J. Med. Econ.* 19(10), 959–964 (2016).
- 14. Evaluates 2537 ablations performed during 2013 and 2014 at hospitals submitting data to the Premier Perspective Hospital Database. Hospital visit costs were estimated and compared between radiofrequency and cryoballoon ablation catheters at sites using both technologies.
14. Roberts M, Russell LB, Paltiel AD, Chambers M, McEwan P, Krahn M. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force–2. *Value Health* 15(6), 804–811 (2012).

- 15 . Osorio J, Hunter T, Bubien RS, Thorington S, Rajendra A, Arciniegas J. A comparison of paroxysmal atrial fibrillation ablation efficiency and clinical outcomes across technologies in a high-volume center. *Europace* 19(3), iii371 (2017).
- **Evaluates 383 ablations (277 ST, 43 SF and 63 CB) performed between July 2013 and June 2016 at a single electrophysiology practice. Reablation rates within 1 year of the index procedure were compared across thermocool smarttouch catheter, SF Catheter and Arctic Front Advance Cryoballoon catheters.**
16. US Bureau of Labor Statistics. Consumer Price Index. www.bls.gov/cpi/
- **Consumer price index tables showing the relative change in cost over time in medical care to allow fair comparison of costs across time.**
17. Kuck KH, Brugada J, Furnkranz A *et al.* Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N. Engl. J. Med.* 374(23), 2235–2245 (2016).
18. Mandell J, Amico F, Parekh S, Snow J, Germano J, Cohen TJ. Early experience with the cryoablation balloon procedure for the treatment of atrial fibrillation by an experienced radiofrequency catheter ablation center. *J. Invasive Cardiol.* 25(6), 288–292 (2013).
- **Analysis of hospital costs from a single site comparing costs between radiofrequency and cryoablation procedures.**
- 19 . Perrone F, Costantini M, Carreras G. Cost–consequence analysis of Thermocool smarttouch catheter for transcatheter ablation of atrial fibrillation in Terni's hospital. *Value Health* 16(3), A284 (2013).

